

operably linked to a promoter which directs expression in [the] a mammary gland, wherein [the] said modified nucleic acid sequence has been modified by replacing one or more AT-containing codons of [the] said modified nucleic acid sequence as it naturally occurs in [the] a parasite with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as [the] a replaced codon as derived from said parasite; and allowing [the] said non-human transgenic mammal to express [the] said parasite protein or fragment thereof in its milk, to thereby produce [a] said parasite protein or fragment thereof.

7. (Twice Amended) A method for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing [a] said non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding [a] said parasite protein or fragment thereof operably linked to a promoter which directs expression in [the] a mammary gland, wherein [the] said nucleic acid sequence of said parasite protein or fragment thereof has been modified by replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence of said parasite protein or fragment thereof as it naturally occurs in [the] a parasite with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of [the] said AUUUA mRNA instability motif; and

allowing [the] said non-human transgenic mammal to express [the] said parasite protein or fragment thereof in its milk, to thereby produce said [a] parasite protein or fragment thereof, and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

8. (Twice Amended) The method of claim 6 or claim 7, wherein more than one codon in [the] a naturally occurring nucleic acid has been replaced [with a preferred mammary gland-specific codon] by more than one codon preferred by a mammalian cell for purposes of expression while encoding the same amino acid sequence as [the] that encoded by said naturally occurring nucleic acid of said parasite protein or fragment thereof [replaced codon].

10. (Twice Amended) A method for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding [a] said parasite protein or fragment thereof operably linked to a promoter which directs expression in [the] a mammary gland, wherein [the] said modified nucleic acid sequence has been modified by:

a) replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence of said parasite protein or fragment thereof as it naturally occurs in [the] a parasite with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of [the] said AUUUA mRNA instability motif; [and]

b) replacing one or more AT-containing codons of [the] said modified nucleic acid sequence as it naturally occurs in [the] said parasite with a [preferred mammary gland-specific] codon or codons

preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as the replaced codon; and  
c) allowing [the] said non-human transgenic mammal to express [the] said parasite protein or fragment thereof in its milk, to thereby produce [a] said parasite protein or fragment thereof and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

20. (Amended) A transgenic non-human mammal whose germline comprises a modified nucleic acid sequence encoding a parasite protein or fragment thereof operably linked to a promoter which directs expression in [the] a mammary gland, wherein [the] said modified nucleic acid sequence has been modified by replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence as it naturally occurs in [the] a parasite with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of [the] said AUUUA mRNA instability motif and by replacing one or more AT-containing codons of the nucleic acid sequence of said parasite protein or fragment thereof as it naturally occurs in the parasite with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as the replaced codon, wherein [the] said non-human transgenic mammal expresses [the] said parasite protein or fragment thereof in its milk and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

31. (Twice Amended) The method of claim 10, wherein [the] said modified nucleic acid sequence has [the same] at least one codon of the naturally occurring nucleic acid sequence of said parasite replaced with a [preferred mammary gland-specific] codon or

codons preferred by a mammalian cell for the purposes of expression such that both the AT content of [the] said nucleic acid sequence of said parasite protein or fragment thereof is lowered relative to that of said naturally occurring nucleic acid sequence of said parasite protein or fragment thereof [is lowered] and the mRNA instability motif of [the] said naturally occurring nucleic acid sequence of said parasite protein or fragment thereof is eliminated by the [preferred mammary gland-specific] utilization of an alternative codon or codons preferred by a mammalian cell for the purposes of expression.

32. (Twice Amended) The method of claim 10, wherein [all] each of [the] said AUUUA mRNA instability motifs present in the naturally occurring nucleic acid have been replaced by a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof.

33. (Twice Amended) The method of claim 10, wherein [the] said modified nucleic acid sequence further comprises at least one additional codon other than [the] a first codon replaced to lower AT content or [the codon replaced] a nucleic acid sequence modification made to eliminate [an] said AUUUA mRNA instability motif which has been replaced with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same parasite protein or fragment thereof as found in the naturally occurring nucleic acid sequence.

34. (Twice Amended) The method of claim 10, wherein all of the codons of the naturally occurring nucleic acid sequence have been replaced with a [preferred mammary gland-specific] codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same parasite protein or fragment thereof as found in the naturally occurring nucleic acid sequence .

35. (Twice Amended) The method of claim 10, wherein [the modified nucleic acid] said parasite protein or fragment thereof is expressed in the milk of said non-human transgenic

mammal [milk] at a level [which is] of at least 0.5 mg/ml [25% more than naturally occurring nucleic acid is expressed under the same conditions].

36. (Twice Amended) The method of claim 10, wherein [the modified nucleic acid] said parasite protein or fragment thereof is expressed in the milk of said non-human transgenic mammal [milk] at a level which is between 1.0 mg/ml and 2.0 mg/ml [at least 50% more than the naturally occurring nucleic acid is expressed under the same conditions].

37. (Twice Amended) The method of claim 10, wherein said parasite protein or fragment thereof as expressed in said non-human transgenic mammal [the modified nucleic acid] can be detectably [is] expressed in the milk of said transgenic non-human mammal [at a level which is at least 100% more than the naturally occurring nucleic acid is expressed under the same conditions].

48. (Amended) The method of claim 10, wherein all non-preferred [mammary gland specific] codons are replaced with a [preferred mammary gland specific codons] codon or codons preferred by a mammalian cell for the purposes of expression.

**Please add claims 49 through 76 as follows:**

49. (New) The parasite protein or fragment thereof as produced by the method of claim 6.

50. (New) The method of claim 6 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.

51. (New) The method of claim 50 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.

52. (New) The method of claim 6 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.

53. (New) The method of claim 6 wherein said promoter is selected from a group of promoters consisting of:

- a) beta-casein;
- b) bovine lactoglobulin;
- c) whey acid promoter;
- d) alpha-ovalbumin; and
- e) caprine casein.

54. (New) The method of claim 6 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:

- a) caprine;
- b) bovine;
- c) porcine;
- d) rodent; and
- e) ovine.

55. (New) The method of claim 6 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.

56. (New) The parasite protein or fragment thereof as produced by the method of claim 7.

57. (New) The method of claim 7 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.

58. (New) The method of claim 57 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.

59. (New) The method of claim 7 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.

60. (New) The method of claim 7 wherein said promoter is selected from a group of promoters consisting of:

- a) beta-casein;
- b) bovine lactoglobulin;
- c) whey acid promoter;
- d) alpha-ovalbumin; and
- e) caprine casein.

61. (New) The method of claim 7 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:

- a) caprine;
- b) bovine;
- c) porcine;
- d) rodent; and
- e) ovine.

62. (New) The method of claim 7 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.

63. (New) The parasite protein or fragment thereof as produced by the method of claim 10.

64. (New) The method of claim 10 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.

65. (New) The method of claim 64 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the Plasmodium falciparum protein MSP-1.
66. (New) The method of claim 10 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.
67. (New) The method of claim 10 wherein said promoter is selected from a group of promoters consisting of:
- a) beta-casein;
  - b) bovine lactoglobulin;
  - c) whey acid promoter;
  - d) alpha-ovalbumin; and
  - e) caprine casein.
68. (New) The method of claim 10 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:
- a) caprine;
  - b) bovine;
  - c) porcine;
  - d) rodent; and
  - e) ovine.
69. (New) The method of claim 10 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.
70. (New) The parasite protein or fragment thereof as produced by the method of claim 20.



71. (New) The method of claim 20 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.
72. (New) The method of claim 71 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.
73. (New) The method of claim 20 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.
74. (New) The method of claim 20 wherein said promoter is selected from a group of promoters consisting of:
- a) beta-casein;
  - b) bovine lactoglobulin;
  - c) whey acid promoter;
  - d) alpha-ovalbumin; and
  - e) caprine casein.
75. (New) The method of claim 20 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:
- a) caprine;
  - b) bovine;
  - c) porcine;
  - d) rodent; and
  - e) ovine.
76. (New) The method of claim 20 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.

## Claim Appendix

6. (Twice Amended) A method for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing said non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland, wherein said modified nucleic acid sequence has been modified by replacing one or more AT-containing codons of said modified nucleic acid sequence as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as a replaced codon as derived from said parasite; and allowing said non-human transgenic mammal to express said parasite protein or fragment thereof in its milk, to thereby produce said parasite protein or fragment thereof.

7. (Twice Amended) A method for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing said non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland, wherein said nucleic acid sequence of said parasite protein or fragment thereof has been modified by replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence of said parasite protein or fragment thereof as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of said AUUUA mRNA instability motif; and

allowing said non-human transgenic mammal to express said parasite protein or fragment thereof in its milk, to thereby produce said parasite protein or fragment thereof, and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

8. (Twice Amended) The method of claim 6 or claim 7, wherein more than one codon in a naturally occurring nucleic acid has been replaced by more than one codon preferred by a mammalian cell for purposes of expression while encoding the same amino acid sequence as that encoded by said naturally occurring nucleic acid of said parasite protein or fragment thereof.

10. (Twice Amended) A method for producing a parasite protein or fragment thereof in the milk of a non-human transgenic mammal, comprising:

providing a non-human transgenic mammal whose genome comprises a modified nucleic acid sequence encoding said parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland, wherein said modified nucleic acid sequence has been modified by:

- a) replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence of said parasite protein or fragment thereof as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of said AUUUA mRNA instability motif;
- b) replacing one or more AT-containing codons of said modified nucleic acid sequence as it naturally occurs in said parasite with a codon or codons preferred by a mammalian cell for the purposes of

expression and encoding the same amino acid as the replaced codon; and

- c) allowing said non-human transgenic mammal to express [the] said parasite protein or fragment thereof in its milk, to thereby produce [a] said parasite protein or fragment thereof and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

20. (Amended) A transgenic non-human mammal whose germline comprises a modified nucleic acid sequence encoding a parasite protein or fragment thereof operably linked to a promoter which directs expression in a mammary gland, wherein said modified nucleic acid sequence has been modified by replacing at least a portion of an AUUUA mRNA instability motif in the coding sequence as it naturally occurs in a parasite with a codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof while encoding the same amino acid as the replaced portion of said AUUUA mRNA instability motif and by replacing one or more AT-containing codons of the nucleic acid sequence of said parasite protein or fragment thereof as it naturally occurs in the parasite with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same amino acid as the replaced codon, wherein said non-human transgenic mammal expresses said parasite protein or fragment thereof in its milk and wherein the naturally occurring nucleic acid sequence encoding said parasite protein or fragment thereof contains at least one AUUUA instability motif.

31. (Twice Amended) The method of claim 10, wherein said modified nucleic acid sequence has at least one codon of the naturally occurring nucleic acid sequence of said parasite replaced with a codon or codons preferred by a mammalian cell for the purposes of expression such that both the AT content of said nucleic acid sequence of said parasite protein or fragment thereof is lowered relative to that of said naturally occurring nucleic

acid sequence of said parasite protein or fragment thereof and the mRNA instability motif of said naturally occurring nucleic acid sequence of said parasite protein or fragment thereof is eliminated by the utilization of an alternative codon or codons preferred by a mammalian cell for the purposes of expression.

32. (Twice Amended) The method of claim 10, wherein each of said AUUUA mRNA instability motifs present in the naturally occurring nucleic acid have been replaced by a codon or codons preferred by a mammalian cell for the purposes of expression so as to remove said AUUUA mRNA instability motif or prevent said AUUUA mRNA instability motif from destabilizing mRNAs encoding said parasite protein or fragment thereof.
33. (Twice Amended) The method of claim 10, wherein said modified nucleic acid sequence further comprises at least one additional codon other than a first codon replaced to lower AT content or a nucleic acid sequence modification made to eliminate said AUUUA mRNA instability motif which has been replaced with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same parasite protein or fragment thereof as found in the naturally occurring nucleic acid sequence .
34. (Twice Amended) The method of claim 10, wherein all of the codons of the naturally occurring nucleic acid sequence have been replaced with a codon or codons preferred by a mammalian cell for the purposes of expression and encoding the same parasite protein or fragment thereof as found in the naturally occurring nucleic acid sequence .
35. (Twice Amended) The method of claim 10, wherein said parasite protein or fragment thereof is expressed in the milk of said non-human transgenic mammal at a level of at least 0.5 mg/ml.
36. (Twice Amended) The method of claim 10, wherein said parasite protein or fragment thereof is expressed in the milk of said non-human transgenic mammal at a level which is between 1.0 mg/ml and 2.0 mg/ml.

37. (Twice Amended) The method of claim 10, wherein said parasite protein or fragment thereof as expressed in said non-human transgenic mammal can be detectably expressed in the milk of said transgenic non-human mammal.
48. (Amended) The method of claim 10, wherein all non-preferred codons are replaced with a codon or codons preferred by a mammalian cell for the purposes of expression.
49. (New) The parasite protein or fragment thereof as produced by the method of claim 6.
50. (New) The method of claim 6 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.
51. (New) The method of claim 50 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.
52. (New) The method of claim 6 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.
53. (New) The method of claim 6 wherein said promoter is selected from a group of promoters consisting of:
- a) beta-casein;
  - b) bovine lactoglobulin;
  - c) whey acid promoter;
  - d) alpha-ovalbumin; and
  - e) caprine casein.
54. (New) The method of claim 6 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:
- a) caprine;
  - b) bovine;
  - c) porcine;

- d) rodent; and
- e) ovine.

55. (New) The method of claim 6 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.
56. (New) The parasite protein or fragment thereof as produced by the method of claim 7.
57. (New) The method of claim 7 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.
58. (New) The method of claim 57 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.
59. (New) The method of claim 7 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.
60. (New) The method of claim 7 wherein said promoter is selected from a group of promoters consisting of:
- a) beta-casein;
  - b) bovine lactoglobulin;
  - c) whey acid promoter;
  - d) alpha-ovalbumin; and
  - e) caprine casein.
61. (New) The method of claim 7 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:
- a) caprine;

- b) bovine;
- c) porcine;
- d) rodent; and
- e) ovine.

62. (New) The method of claim 7 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.
63. (New) The parasite protein or fragment thereof as produced by the method of claim 10.
64. (New) The method of claim 10 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.
65. (New) The method of claim 64 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.
66. (New) The method of claim 10 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.
67. (New) The method of claim 10 wherein said promoter is selected from a group of promoters consisting of:
- a) beta-casein;
  - b) bovine lactoglobulin;
  - c) whey acid promoter;
  - d) alpha-ovalbumin; and
  - e) caprine casein.



68. (New) The method of claim 10 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:

- a) caprine;
- b) bovine;
- c) porcine;
- d) rodent; and
- e) ovine.

69. (New) The method of claim 10 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.

70. (New) The parasite protein or fragment thereof as produced by the method of claim 20.

71. (New) The method of claim 20 wherein said parasite protein or fragment thereof is a protein fragment derived from the parasite *Plasmodium falciparum*.

72. (New) The method of claim 71 wherein said parasite protein or fragment thereof is a protein, polypeptide or peptide derived from the *Plasmodium falciparum* protein MSP-1.

73. (New) The method of claim 20 wherein said mammalian cell for the purposes of expression is a mammary epithelial cell.

74. (New) The method of claim 20 wherein said promoter is selected from a group of promoters consisting of:

- a) beta-casein;
- b) bovine lactoglobulin;
- c) whey acid promoter;
- d) alpha-ovalbumin; and

e) caprine casein.

75. (New) The method of claim 20 wherein said non-human transgenic mammal is selected from a group of mammals consisting of:

- a) caprine;
- b) bovine;
- c) porcine;
- d) rodent; and
- e) ovine.

76. (New) The method of claim 20 wherein said modified nucleic acid sequence is modified to provide for the expression of a modified amino acid sequence such that there is at least one Asparagine to Glutamine change to eliminate at least one glycosylation site on said parasite protein or protein fragment thereof produced by said non-human transgenic mammal.